1 Rec'd PCT/PTO 13 FEB 2006 10/533299

Sequence listing

<110> Pieris Proteolab AG

<120> Soluble truncated polypeptides of the Nogo-A protein, methods for the production of such polypeptides and methods for identifying compounds having detectable affinity to a Nogo-A protein

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Arg Gly Pro Leu Pro Ala Ala Pro Pro Ala Ala Pro Glu A	Arg Gln 105											
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Asp Leu Met Glu Gln Pro Gly Asn Thr Val Ser Ser Gly	Gln Glu											

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Gly As	n Leu	Ser	Ala 245	Val	Ser	Ser	Ser	Glu 250	Gly	Thr	Ile	Glu	Glu 255
Thr Le	eu Asn	Glu	Ala 260	Ser	Lys	Glu	Leu	Pro 265	Glu	Arg	Ala	Thr	Asn 270
Pro Ph	ne Val	Asn	Arg 275	Asp	Leu	Ala	Glu	Phe 280	Ser	Glu	Leu	Glu	Tyr 285
Ser Gl	u Met	Gly	Ser 290	Ser	Phe	Lys	Gly	Ser 295	Pro	Lys	Gly	Glu	Ser 310
Ala Il	e Lev	Val	Glu 305	Asn	Thr	Lys	Glu	Glu 310	Val	Ile	Val	Arg	Ser 315
Lys As	sp Lys	Glu	Asp 320	Leu	Val	Cys	Ser	Ala 325	Ala	Leu	His	Ser	Pro 330
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Asp Se	er Leu	ı Glu	Gln 410	Lys	Ser	Leu	Gly	Lys 415	Asp	Ser	Glu	Gly	Arg 420
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Glu Se	er Thi	Thr	Ala 455	Asn	Thr	Phe	Pro	Leu 460	Leu	Glu	Asp	His	Thr 465
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Leu Va	al Ala	a Val	Gln 500	Asp	Ser	Glu	Ala	Asp 505	Tyr	Val	Thr	Thr	Asp 510

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190

185

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Gln	Glu	Ala	Cys	Glu 560	Ser	Glu	Leu	Asn	Glu 565	Val	Thr	Gly	Thr	Lys 570
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Glu	Ile	Lys	Glu	Pro 680	Glu	Asn	Ile	Asn	Ala 685	Ala	Leu	Gln	Glu	Thr 690
Glu	Ala	Pro	Tyr	Ile 695	Ser	Ile	Ala	Cys	Asp 700	Leu	Ile	Lys	Glu	Thr 705
Lys	Leu	Ser	Ala	Glu 710	Pro	Ala	Pro	Glu	Phe 715	Ser	Asp	Tyr	Ser	Glu 720
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Glu	Asp	Ser	Ser	Pro 740	Asp	Ser	Glu	Pro	Val 745	Asp	Leu	Phe	Ser	Asp 750
Asp	Ser	Ile	Pro	Asp 755	Val	Pro	Gln	Lys	Gln 760	Asp	Glu	Thr	Val	Met 765
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11

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                                                             50
                                                             66
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Glu Trp Ile Gly Asp Ile Tyr Pro Gly Gly Gly Tyr Thr Asn Tyr
Asn Glu Lys Phe Lys Gly Lys Ala Thr Leu Thr Ala Asp Thr Ser
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Ser Ser Thr Ala Tyr Met Gln Leu Ser Ser Leu Thr Ser Glu Asp
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                 80
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Leu Leu Ile Tyr Gly Ala Thr Asn Leu Ala Asp Gly Met Ser Ser
Arg Phe Ser Gly Ser Gly Ser Gly Arg Gln Tyr Ser Leu Lys Ile
                 65
Ser Ser Leu His Pro Asp Asp Val Ala Thr Tyr Tyr Cys Gln Asn
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Ala Val Ala Leu Ala Gly Phe Ala Thr Val Ala Gln Ala Ser Phe
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Lys Glu His Gly Tyr Leu Gly Asn Leu Ser Ala Val Ser Ser Ser
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Glu Gly Thr Ile Glu Glu Thr Leu Asn Glu Ala Ser Lys Glu Leu
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Pro Glu Arg Ala Thr Asn Pro Phe Val Asn Arg Asp Leu Ala Glu
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ttt tca qaa tta qaa tat tca qaa atg gga tca tct ttt aaa ggc 270
Phe Ser Glu Leu Glu Tyr Ser Glu Met Gly Ser Ser Phe Lys Gly
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tcc cca aaa gga gag tca gcc ata tta gta gaa aac act aag gaa 315
Ser Pro Lys Gly Glu Ser Ala Ile Leu Val Glu Asn Thr Lys Glu
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gaa gta att gtg agg agt aaa gac aaa gag gat tta gtt tgt agt 360
Glu Val Ile Val Arg Ser Lys Asp Lys Glu Asp Leu Val Cys Ser
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gca gcc ctt cac agt cca caa gaa tca cct gtg ggt aaa gaa gac 405
Ala Ala Leu His Ser Pro Gln Glu Ser Pro Val Gly Lys Glu Asp
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Arg Val Val Ser Pro Glu Lys Thr Met Asp Ile Phe Asn Glu Met
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Gln Met Ser Val Val Ala Pro Val Arg Glu Glu Tyr Ala Asp Phe
        125
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595
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gat toa tot cog att gag ata ata gat gaa ttt coc acg ttt gtc 1935
Asp Ser Ser Pro Ile Glu Ile Ile Asp Glu Phe Pro Thr Phe Val
        605
                            610
agt gct aaa gat gat tct cct aaa tta gcc aag gag tac act gat 1980
Ser Ala Lys Asp Asp Ser Pro Lys Leu Ala Lys Glu Tyr Thr Asp
        620
                            625
cta gaa gta tcc gac aaa agt gaa att gct aat atc caa agc ggg 2025
Leu Glu Val Ser Asp Lys Ser Glu Ile Ala Asn Ile Gln Ser Gly
qca qat tca ttq cct tqc tta gaa ttq ccc tqt gac ctt tct ttc 2070
Ala Asp Ser Leu Pro Cys Leu Glu Leu Pro Cys Asp Leu Ser Phe
        650
aag aat ata tat cct aaa gat gaa gta cat gtt tca gat gaa ttc 2115
Lys Asn Ile Tyr Pro Lys Asp Glu Val His Val Ser Asp Glu Phe
tcc gaa aat agg tcc agt gta tct aag gca tcc ata tcg cct tca 2160
Ser Glu Asn Arg Ser Ser Val Ser Lys Ala Ser Ile Ser Pro Ser
                            685
aat gtc tct gct ttg gaa cct cag aca gaa atg ggc agc ata gtt 2205
Asn Val Ser Ala Leu Glu Pro Gln Thr Glu Met Gly Ser Ile Val
                                                             2248
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Lys Ser Ala Trp Arg His Pro Gln Phe Gly Gly End
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ctt ttt go Leu Phe Al											135
gca gaa aa Ala Glu Ly											180
tcg tct gg Ser Ser Gl											225
gcc tct ct Ala Ser Le	t cct tct eu Pro Ser 50	cta tct Leu Ser	cct Pro 55	ctc Leu	tca Ser	act Thr	gtt Val	tct Ser 60	ttt Phe	aaa Lys	270
gaa cat go Glu His Gl	ga tac ctt .y Tyr Leu 55	ggt aac Gly Asn	tta Leu 70	tca Ser	gca Ala	gtg Val	tca Ser	tcc Ser 75	tca Ser	gaa Glu	315
gga aca at Gly Thr II	t gaa gaa Le Glu Glu 80	act tta Thr Leu	aat Asn 85	gaa Glu	gct Ala	tct Ser	aaa Lys	gag Glu 90	ttg Leu	cca Pro	360
gag agg go Glu Arg Al	ca aca aat .a Thr Asn 95	cca ttt Pro Phe	gta Val 100	aat Asn	aga Arg	gat Asp	tta Leu	gca Ala 105	gaa Glu	ttt Phe	405
tca gaa tt Ser Glu Le 1:	eu Glu Tyr	tca gaa Ser Glu	atg Met 115	gga Gly	tca Ser	tct Ser	ttt Phe	aaa Lys 120	ggc Gly	tcc Ser	450
	ga gag tca Ly Glu Ser 25	gcc ata Ala Ile	tta Leu 130	gta Val	gaa Glu	aac Asn	act Thr	aag Lys 135	gaa Glu	gaa Glu	495
gta att gt Val Ile Va 14	ig agg agt al Arg Ser 10	aaa gac Lys Asp	aaa Lys 145	gag Glu	gat Asp	tta Leu	gtt Val	tgt Cys 150	agt Ser	gca Ala	540
gcc ctt ca Ala Leu H: 1	ac agt cca is Ser Pro 55	caa gaa Gln Glu	tca Ser 160	cct Pro	gtg Val	ggt Gly	aaa Lys	gaa Glu 165	gac Asp	aga Arg	585
gtt gtg to Val Val So 1	ct cca gaa er Pro Glu 70	aag aca Lys Thr	atg Met 175	gac Asp	att Ile	ttt Phe	aat Asn	gaa Glu 180	atg Met	cag Gln	630
atg tca g	ta gta gca	cct gtg	agg	gaa	gag	tat	gca	gac	ttt	aag	675

Met Ser Val Val Ala Pro Val Arg Glu Glu Tyr Ala Asp Phe Lys 190 cca ttt gaa caa gca tgg gaa gtg aaa gat act tat gag gga agt 720 Pro Phe Glu Gln Ala Trp Glu Val Lys Asp Thr Tyr Glu Gly Ser 205 agg gat gtg ctg gct gct aga gct aat gtg gaa agt aaa gtg gac 765 Arg Asp Val Leu Ala Ala Arg Ala Asn Val Glu Ser Lys Val Asp 220 225 aga aaa tgc ttg gaa gat agc ctg gag caa aaa agt ctt ggg aag 810 Arg Lys Cys Leu Glu Asp Ser Leu Glu Gln Lys Ser Leu Gly Lys 235 gat agt gaa ggc aga aat gag gat gct tct ttc ccc agt acc cca 855 Asp Ser Glu Gly Arg Asn Glu Asp Ala Ser Phe Pro Ser Thr Pro 245 250 gaa cct gtg aag gac agc tcc aga gca tat att acc tgt gct tcc 900 Glu Pro Val Lys Asp Ser Ser Arg Ala Tyr Ile Thr Cys Ala Ser 265 260 ttt acc tca qca acc gaa agc acc aca gca aac act ttc cct ttg 945 Phe Thr Ser Ala Thr Glu Ser Thr Thr Ala Asn Thr Phe Pro Leu 285 280 275 tta gaa gat cat act tca gaa aat aaa aca gat gaa aaa aaa ata 990 Leu Glu Asp His Thr Ser Glu Asn Lys Thr Asp Glu Lys Lys Ile 300 295 290 gaa gaa agg aag gcc caa att ata aca gag aag act agc ccc aaa 1035 Glu Glu Arg Lys Ala Gln Ile Ile Thr Glu Lys Thr Ser Pro Lys 315 305 310 acg tca aat cct ttc ctt gta gca gta cag gat tct gag gca gat 1080 Thr Ser Asn Pro Phe Leu Val Ala Val Gln Asp Ser Glu Ala Asp 320 325 330 tat gtt aca aca gat acc tta tca aag gtg act gag gca gca gtg 1125 Tyr Val Thr Thr Asp Thr Leu Ser Lys Val Thr Glu Ala Ala Val 345 340 335 tca aac atg cct gaa ggt ctg acg cca gat tta gtt cag gaa gca 1170 Ser Asn Met Pro Glu Gly Leu Thr Pro Asp Leu Val Gln Glu Ala 355 360 350 tgt gaa agt gaa ctg aat gaa gcc aca ggt aca aag att gct tat 1215 Cys Glu Ser Glu Leu Asn Glu Ala Thr Gly Thr Lys Ile Ala Tyr 365 370 gaa aca aaa gtg gac ttg gtc caa aca tca gaa gct ata caa gaa 1260 Glu Thr Lys Val Asp Leu Val Gln Thr Ser Glu Ala Ile Gln Glu 390 385 380 tca ctt tac ccc aca gca cag ctt tgc cca tca ttt gag gaa gct 1305 Ser Leu Tyr Pro Thr Ala Gln Leu Cys Pro Ser Phe Glu Glu Ala 395 gaa gca act ccg tca cca gtt ttg cct gat att gtt atg gaa gca 1350 Glu Ala Thr Pro Ser Pro Val Leu Pro Asp Ile Val Met Glu Ala

410		415	420	
cca tta aat tct Pro Leu Asn Ser 425				
ccc agt gta tcc Pro Ser Val Ser 440				
agt ata aag ctt Ser Ile Lys Leu 455				
atg aat gta gca Met Asn Val Ala 470				
gag cct gaa agt Glu Pro Glu Ser 485	ttt aat gca Phe Asn Ala	gct gtt ca Ala Val Gl 490	g gaa aca gaa n Glu Thr Glu 495	gct cct 1575 Ala Pro
tat ata tcc att Tyr Ile Ser Ile 500				
act gag cca agt Thr Glu Pro Ser 515				
ttc gag aag tcg Phe Glu Lys Ser 530	gtg ccc gaa Val Pro Glu	cac gct ga His Ala Gl 535	g cta gtg gag u Leu Val Glu 540	gat tcc 1710 Asp Ser
tca cct gaa tct Ser Pro Glu Ser 545				
cct gaa gtc cca Pro Glu Val Pro 560	caa aca caa Gln Thr Gln	gag gag gc Glu Glu Al 565	t gtg atg ctc a Val Met Leu 570	atg aag 1800 Met Lys
gag agt ctc act Glu Ser Leu Thr 575				
gag aga ctt agt Glu Arg Leu Ser 590				
gag tct ttt cag Glu Ser Phe Gln 605				
aat gac att cca Asn Asp Ile Pro 620				
atg gaa gag ttt Met Glu Glu Phe 635				

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tct tct aag gaa gac aaa ata aaa gaa agt gaa aca ttt tca gat 2070
Ser Ser Lys Glu Asp Lys Ile Lys Glu Ser Glu Thr Phe Ser Asp
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        650
tca tct ccg att gag ata ata gat gaa ttt ccc acg ttt gtc agt 2115
Ser Ser Pro Ile Glu Ile Ile Asp Glu Phe Pro Thr Phe Val Ser
                            670
gct aaa gat gat tct cct aaa tta gcc aag gag tac act gat cta 2160
Ala Lys Asp Asp Ser Pro Lys Leu Ala Lys Glu Tyr Thr Asp Leu
                            685
gaa gta tcc gac aaa agt gaa att gct aat atc caa agc ggg gca 2205
Glu Val Ser Asp Lys Ser Glu Ile Ala Asn Ile Gln Ser Gly Ala
                            700
        695
gat tca ttg cct tgc tta gaa ttg ccc tgt gac ctt tct ttc aag 2250
Asp Ser Leu Pro Cys Leu Glu Leu Pro Cys Asp Leu Ser Phe Lys
        710
                            715
aat ata tat cct aaa gat gaa gta cat gtt tca gat gaa ttc tcc 2295
Asn Ile Tyr Pro Lys Asp Glu Val His Val Ser Asp Glu Phe Ser
                                                 735
        725
                            730
gaa aat agg tcc agt gta tct aag gca tcc ata tcg cct tca aat 2340
Glu Asn Arg Ser Ser Val Ser Lys Ala Ser Ile Ser Pro Ser Asn
                                                 750
                            745
        740
gtc tct gct ttg gaa cct cag aca gaa atg ggc agc ata gtt aaa 2385
Val Ser Ala Leu Glu Pro Gln Thr Glu Met Gly Ser Ile Val Lys
        755
                            760
                                                 765
agc gct tgg cgt cac ccg cag ttc ggt ggt taa taa gctt
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Ser Ala Trp Arg His Pro Gln Phe Gly Gly End
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hexahistidine tag
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gaa caa gca tgg gaa gtg aaa gat act tat gag gga agt agg gat 585 Glu Gln Ala Trp Glu Val Lys Asp Thr Tyr Glu Gly Ser Arg Asp 160 gtg ctg gct gct aga gct aat gtg gaa agt aaa gtg gac aga aaa 630 Val Leu Ala Ala Arg Ala Asn Val Glu Ser Lys Val Asp Arg Lys 175 tgc ttg gaa gat agc ctg gag caa aaa agt ctt ggg aag gat agt 675 Cys Leu Glu Asp Ser Leu Glu Gln Lys Ser Leu Gly Lys Asp Ser gaa ggc aga aat gag gat gct tct ttc ccc agt acc cca gaa cct 720 Glu Gly Arg Asn Glu Asp Ala Ser Phe Pro Ser Thr Pro Glu Pro 200 gtg aag gac agc tcc aga gca tat att acc tgt gct tcc ttt acc 765 Val Lys Asp Ser Ser Arg Ala Tyr Ile Thr Cys Ala Ser Phe Thr 215 tca gca acc gaa agc acc aca gca aac act ttc cct ttg tta gaa 810 Ser Ala Thr Glu Ser Thr Thr Ala Asn Thr Phe Pro Leu Glu 230 235 gat cat act tca gaa aat aaa aca gat gaa aaa aaa ata gaa gaa 855 Asp His Thr Ser Glu Asn Lys Thr Asp Glu Lys Lys Ile Glu Glu 245 250 agg aag gcc caa att ata aca gag aag act agc ccc aaa acg tca 900 Arg Lys Ala Gln Ile Ile Thr Glu Lys Thr Ser Pro Lys Thr Ser 265 aat cct ttc ctt gta gca gta cag gat tct gag gca gat tat gtt 945 Asn Pro Phe Leu Val Ala Val Gln Asp Ser Glu Ala Asp Tyr Val 280 aca aca gat acc tta tca aag gtg act gag gca gca gtg tca aac 990 Thr Thr Asp Thr Leu Ser Lys Val Thr Glu Ala Ala Val Ser Asn 295 atg cct gaa ggt ctg acg cca gat tta gtt cag gaa gca tgt gaa 1035 Met Pro Glu Gly Leu Thr Pro Asp Leu Val Gln Glu Ala Cys Glu 310 agt gaa ctg aat gaa gcc aca ggt aca aag att gct tat gaa aca 1080 Ser Glu Leu Asn Glu Ala Thr Gly Thr Lys Ile Ala Tyr Glu Thr 325 aaa gtg gac ttg gtc caa aca tca gaa gct ata caa gaa tca ctt 1125 Lys Val Asp Leu Val Gln Thr Ser Glu Ala Ile Gln Glu Ser Leu 340 tac ccc aca gca cag ctt tgc cca tca ttt gag gaa gct gaa gca 1170 Tyr Pro Thr Ala Gln Leu Cys Pro Ser Phe Glu Glu Ala Glu Ala 355 act ccg tca cca gtt ttg cct gat att gtt atg gaa gca cca tta 1215 Thr Pro Ser Pro Val Leu Pro Asp Ile Val Met Glu Ala Pro Leu 370 aat tot otc ott oca ago got ggt got tot gta gtg cag coc agt 1260

2

Asn Ser Leu Leu Pro Ser Ala Gly Ala Ser Val Val Gln Pro Ser 385 gta tcc cca ctg gaa gca cct cct cca gtt agt tat gac agt ata 1305 Val Ser Pro Leu Glu Ala Pro Pro Pro Val Ser Tyr Asp Ser Ile 400 aag ctt gag cct gaa aac ccc cca cca tat gaa gaa gcc atg aat 1350 Lys Leu Glu Pro Glu Asn Pro Pro Pro Tyr Glu Glu Ala Met Asn 415 410 gta gca cta aaa gct ttg gga aca aag gaa gga ata aaa gag cct 1395 Val Ala Leu Lys Ala Leu Gly Thr Lys Glu Gly Ile Lys Glu Pro 430 425 gaa agt ttt aat gca gct gtt cag gaa aca gaa gct cct tat ata 1440 Glu Ser Phe Asn Ala Ala Val Gln Glu Thr Glu Ala Pro Tyr Ile 440 445 450 tcc att gcg tgt gat tta att aaa gaa aca aag ctc tcc act gag 1485 Ser Ile Ala Cys Asp Leu Ile Lys Glu Thr Lys Leu Ser Thr Glu 460 465 455 cca agt cca gat ttc tct aat tat tca gaa ata gca aaa ttc gag 1530 Pro Ser Pro Asp Phe Ser Asn Tyr Ser Glu Ile Ala Lys Phe Glu 480 475 470 aag tcg gtg ccc gaa cac gct gag cta gtg gag gat tcc tca cct 1575 Lys Ser Val Pro Glu His Ala Glu Leu Val Glu Asp Ser Ser Pro 490 495 485 gaa tot gaa coa gtt gac tta ttt agt gat gat tog att cot gaa 1620 Glu Ser Glu Pro Val Asp Leu Phe Ser Asp Asp Ser Ile Pro Glu 500 505 510 gtc cca caa aca caa gag gag gct gtg atg ctc atg aag gag agt 1665 Val Pro Gln Thr Gln Glu Glu Ala Val Met Leu Met Lys Glu Ser 520 525 515 ctc act gaa gtg tct gag aca gta gcc cag cac aaa gag gag aga 1710 Leu Thr Glu Val Ser Glu Thr Val Ala Gln His Lys Glu Glu Arg 535 530 ctt agt gcc tca cct cag gag cta gga aag cca tat tta gag tct 1755 Leu Ser Ala Ser Pro Gln Glu Leu Gly Lys Pro Tyr Leu Glu Ser 545 550 ttt cag ccc aat tta cat agt aca aaa gat gct gca tct aat gac 1800 Phe Gln Pro Asn Leu His Ser Thr Lys Asp Ala Ala Ser Asn Asp 560 565 att cca aca ttg acc aaa aag gag aaa att tct ttg caa atg gaa 1845 Ile Pro Thr Leu Thr Lys Lys Glu Lys Ile Ser Leu Gln Met Glu 575 gag ttt aat act gca att tat tca aat gat gac tta ctt tct tct 1890 Glu Phe Asn Thr Ala Ile Tyr Ser Asn Asp Asp Leu Leu Ser Ser 590 595 aag gaa gac aaa ata aaa gaa agt gaa aca ttt tca gat tca tct 1935 Lys Glu Asp Lys Ile Lys Glu Ser Glu Thr Phe Ser Asp Ser Ser

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610
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ccg att gag ata ata gat gaa ttt ccc acg ttt gtc agt gct aaa 1980
Pro Ile Glu Ile Ile Asp Glu Phe Pro Thr Phe Val Ser Ala Lys
                            625
        620
gat gat tct cct aaa tta gcc aag gag tac act gat cta gaa gta 2025
Asp Asp Ser Pro Lys Leu Ala Lys Glu Tyr Thr Asp Leu Glu Val
        635
                            640
tcc gac aaa agt gaa att gct aat atc caa agc ggg gca gat tca 2070
Ser Asp Lys Ser Glu Ile Ala Asn Ile Gln Ser Gly Ala Asp Ser
        650
ttg cct tgc tta gaa ttg ccc tgt gac ctt tct ttc aag aat ata 2115
Leu Pro Cys Leu Glu Leu Pro Cys Asp Leu Ser Phe Lys Asn Ile
        665
tat cct aaa gat gaa gta cat gtt tca gat gaa ttc tcc gaa aat 2160
Tyr Pro Lys Asp Glu Val His Val Ser Asp Glu Phe Ser Glu Asn
        680
                            685
agg tcc agt gta tct aag gca tcc ata tcg cct tca aat gtc tct 2205
Arg Ser Ser Val Ser Lys Ala Ser Ile Ser Pro Ser Asn Val Ser
                            700
        695
gct ttg gaa cct cag aca gaa atg ggc agc ata gtt aaa agc gct 2250
Ala Leu Glu Pro Gln Thr Glu Met Gly Ser Ile Val Lys Ser Ala
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                                                             2278
cac cat cac cat cac cat taa taa gctt
His His His His His End
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3

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265 270 260 Phe Thr Ser Ala Thr Glu Ser Thr Thr Ala Asn Thr Phe Pro Leu 280 Leu Glu Asp His Thr Ser Glu Asn Lys Thr Asp Glu Lys Lys Ile 295 Glu Glu Arg Lys Ala Gln Ile Ile Thr Glu Lys Thr Ser Pro Lys 310 Thr Ser Asn Pro Phe Leu Val Ala Val Gln Asp Ser Glu Ala Asp 325 Tyr Val Thr Thr Asp Thr Leu Ser Lys Val Thr Glu Ala Ala Val 340 335 Ser Asn Met Pro Glu Gly Leu Thr Pro Asp Leu Val Gln Glu Ala 355 350 Cys Glu Ser Glu Leu Asn Glu Ala Thr Gly Thr Lys Ile Ala Tyr 370 365 Glu Thr Lys Val Asp Leu Val Gln Thr Ser Glu Ala Ile Gln Glu 385 Ser Leu Tyr Pro Thr Ala Gln Leu Cys Pro Ser Phe Glu Glu Ala 395 400 Glu Ala Thr Pro Ser Pro Val Leu Pro Asp Ile Val Met Glu Ala 415 Pro Leu Asn Ser Leu Leu Pro Ser Ala Gly Ala Ser Val Val Gln 430 425 Pro Ser Val Ser Pro Leu Glu Ala Pro Pro Pro Val Ser Tyr Asp Ser Ile Lys Leu Glu Pro Glu Asn Pro Pro Pro Tyr Glu Glu Ala 455 Met Asn Val Ala Leu Lys Ala Leu Gly Thr Lys Glu Gly Ile Lys Glu Pro Glu Ser Phe Asn Ala Ala Val Gln Glu Thr Glu Ala Pro 485 Tyr Ile Ser Ile Ala Cys Asp Leu Ile Lys Glu Thr Lys Leu Ser 505 Thr Glu Pro Ser Pro Asp Phe Ser Asn Tyr Ser Glu Ile Ala Lys 515 520 Phe Glu Lys Ser Val Pro Glu His Ala Glu Leu Val Glu Asp Ser 535 Ser Pro Glu Ser Glu Pro Val Asp Leu Phe Ser Asp Asp Ser Ile 545 Pro Glu Val Pro Gln Thr Gln Glu Glu Ala Val Met Leu Met Lys 570 560 565

Glu Ser Leu Thr Glu Val Ser Glu Thr Val Ala Gln His Lys Glu

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Glu Arg Leu Ser Ala Ser Pro Gln Glu Leu Gly Lys Pro Tyr Leu
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Glu Ser Phe Gln Pro Asn Leu His Ser Thr Lys Asp Ala Ala Ser
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Met Glu Glu Phe Asn Thr Ala Ile Tyr Ser Asn Asp Asp Leu Leu
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Ser Ser Pro Ile Glu Ile Ile Asp Glu Phe Pro Thr Phe Val Ser
                            670
Ala Lys Asp Asp Ser Pro Lys Leu Ala Lys Glu Tyr Thr Asp Leu
                            685
        680
Glu Val Ser Asp Lys Ser Glu Ile Ala Asn Ile Gln Ser Gly Ala
                            700
Asp Ser Leu Pro Cys Leu Glu Leu Pro Cys Asp Leu Ser Phe Lys
                            715
        710
Asn Ile Tyr Pro Lys Asp Glu Val His Val Ser Asp Glu Phe Ser
                            730
        725
Glu Asn Arg Ser Ser Val Ser Lys Ala Ser Ile Ser Pro Ser Asn
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28

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Glu Gly Thr Ile Glu Glu Thr Leu Asn Glu Ala Ser Lys Glu Leu
Pro Glu Arg Ala Thr Asn Pro Phe Val Asn Arg Asp Leu Ala Glu
                             40
Phe Ser Glu Leu Glu Tyr Ser Glu Met Gly Ser Ser Phe Lys Gly
Ser Pro Lys Gly Glu Ser Ala Ile Leu Val Glu Asn Thr Lys Glu
Glu Val Ile Val Arg Ser Lys Asp Lys Glu Asp Leu Val Cys Ser
                             85
Ala Ala Leu His Ser Pro Gln Glu Ser Pro Val Gly Lys Glu Asp
                            100
Arg Val Val Ser Pro Glu Lys Thr Met Asp Ile Phe Asn Glu Met
                            115
        110
Gln Met Ser Val Val Ala Pro Val Arg Glu Glu Tyr Ala Asp Phe
                            130
Lys Pro Phe Glu Gln Ala Trp Glu Val Lys Asp Thr Tyr Glu Gly
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                            145
Ser Arg Asp Val Leu Ala Ala Arg Ala Asn Val Glu Ser Lys Val
Asp Arg Lys Cys Leu Glu Asp Ser Leu Glu Gln Lys Ser Leu Gly
Lys Asp Ser Glu Gly Arg Asn Glu Asp Ala Ser Phe Pro Ser Thr
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Pro Glu Pro Val Lys Asp Ser Ser Arg Ala Tyr Ile Thr Cys Ala
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Ser Phe Thr Ser Ala Thr Glu Ser Thr Thr Ala Asn Thr Phe Pro
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220

225

215

Leu Leu Glu Asp His Thr Ser Glu Asn Lys Thr Asp Glu Lys Lys 235 Ile Glu Glu Arq Lys Ala Gln Ile Ile Thr Glu Lys Thr Ser Pro 250 Lys Thr Ser Asn Pro Phe Leu Val Ala Val Gln Asp Ser Glu Ala 265 Asp Tyr Val Thr Thr Asp Thr Leu Ser Lys Val Thr Glu Ala Ala 280 Val Ser Asn Met Pro Glu Gly Leu Thr Pro Asp Leu Val Gln Glu 295 Ala Cys Glu Ser Glu Leu Asn Glu Ala Thr Gly Thr Lys Ile Ala 305 310 Tyr Glu Thr Lys Val Asp Leu Val Gln Thr Ser Glu Ala Ile Gln 325 Glu Ser Leu Tyr Pro Thr Ala Gln Leu Cys Pro Ser Phe Glu Glu 340 335 Ala Glu Ala Thr Pro Ser Pro Val Leu Pro Asp Ile Val Met Glu 355 Ala Pro Leu Asn Ser Leu Leu Pro Ser Ala Gly Ala Ser Val Val 370 365 Gln Pro Ser Val Ser Pro Leu Glu Ala Pro Pro Pro Val Ser Tyr 385 Asp Ser Ile Lys Leu Glu Pro Glu Asn Pro Pro Pro Tyr Glu Glu 395 400 Ala Met Asn Val Ala Leu Lys Ala Leu Gly Thr Lys Glu Gly Ile 415 Lys Glu Pro Glu Ser Phe Asn Ala Ala Val Gln Glu Thr Glu Ala 430 425 Pro Tyr Ile Ser Ile Ala Cys Asp Leu Ile Lys Glu Thr Lys Leu Ser Thr Glu Pro Ser Pro Asp Phe Ser Asn Tyr Ser Glu Ile Ala 455 Lys Phe Glu Lys Ser Val Pro Glu His Ala Glu Leu Val Glu Asp 475 Ser Ser Pro Glu Ser Glu Pro Val Asp Leu Phe Ser Asp Asp Ser 490 485 Ile Pro Glu Val Pro Gln Thr Gln Glu Glu Ala Val Met Leu Met 505 Lys Glu Ser Leu Thr Glu Val Ser Glu Thr Val Ala Gln His Lys 515 520

Glu Glu Arg Leu Ser Ala Ser Pro Gln Glu Leu Gly Lys Pro Tyr 535 Leu Glu Ser Phe Gln Pro Asn Leu His Ser Thr Lys Asp Ala Ala 550 Ser Asn Asp Ile Pro Thr Leu Thr Lys Lys Glu Lys Ile Ser Leu 565 Gln Met Glu Glu Phe Asn Thr Ala Ile Tyr Ser Asn Asp Asp Leu 580 Leu Ser Ser Lys Glu Asp Lys Ile Lys Glu Ser Glu Thr Phe Ser 595 Asp Ser Ser Pro Ile Glu Ile Ile Asp Glu Phe Pro Thr Phe Val Ser Ala Lys Asp Asp Ser Pro Lys Leu Ala Lys Glu Tyr Thr Asp Leu Glu Val Ser Asp Lys Ser Glu Ile Ala Asn Ile Gln Ser Gly Ala Asp Ser Leu Pro Cys Leu Glu Leu Pro Cys Asp Leu Ser Phe 650 655 Lys Asn Ile Tyr Pro Lys Asp Glu Val His Val Ser Asp Glu Phe 670 Ser Glu Asn Arg Ser Ser Val Ser Lys Ala Ser Ile Ser Pro Ser 685 Asn Val Ser Ala Leu Glu Pro Gln Thr Glu Met Gly Ser Ile Val Lys Ser Ala Trp Arg His Pro Gln Phe Gly Gly

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710